Ser. No. 10/075,733
Filed: February 14, 2002

REMARKS

Claims 1-23, 25, 26, 42-44 and 47 are now in this Application, and are presented for the Examiner's consideration.

A final Office Action was mailed October 29, 2003 in the above application.

A Notice of Appeal was filed February 14, 2004, with a three month extension of time.

A Request for Continued Examination (RCE) under 37 C.F.R. §1.114 is being filed concurrently herewith.

This Preliminary Amendment is therefore submitted in the RCE application and specifically responds to the rejections in the final Office Action mailed October 29, 2004.

Prior Art Rejection

Claims 1-4, 6, 10-12, 19, 21, 25 and 43 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,524,481 to Zha et al.

Background

The hollow fiber membrane modules according to the present invention belong to a specific type of module, termed an "immersion module," and are particularly useful in sterile fermentation vessels. During such fermentation, the membrane pores are often blocked due to the deposit of particles or cells out of the feed-solution. This process is termed "fouling" and leads to a malfunction of the membranes. This malfunction of membranes then makes it impossible to control the fermentation process.

Further, if the fermentation requires sterile conditions, the vessels cannot be opened to either remove the deposits or exchange the membrane modules.

Consequently, there is a need to provide a technique that assures the desired functioning of the membranes during the entire time of the fermentation procedure.

The present invention provides a membrane module with almost constant properties over the entire time of a sterile fermentation process. This results in a more efficient sterile fermentation process, a more reliable control of the process and effectively lower costs. The solution provided by the present invention is achieved by using <u>smaller</u> packing densities of the membranes, compared to what is known in the art, in combination with a special housing architecture.

Because of these <u>smaller</u> packing densities, the principle of the present invention is different from what is known in the prior art. Specifically, the present invention prevents fouling due to a) movement of the membranes and b) turbulent flow around the membranes. Both are achieved by a complex interaction of the flow created due to the stirring of the feed solution, the low packing density and the housing architecture of the present membrane module.

With the above in mind, the inventors herein experimented to find the right combinations of packing densities and housing parameters. The open surface areas on the housing as well as on the segmentation elements were found to be necessary in order to allow a turbulent flow around the membranes. The segmentation elements are also required to stabilize the housing. Therefore, the architecture of the housing is particularly adapted to the anti-fouling arrangement according to the present invention. If there is no housing, or if the housing is different from what is disclosed in the present invention, the membranes may be damaged or less efficient.

It is noted that experiments were also conducted with higher packing densities as suggested in the prior art. While being more efficient at the very beginning of the fermentation process, such high packing densities soon resulted in closed membrane pores and even stuck membranes. Such membranes are not effective over the entire fermentation process, and were therefore not adapted for use under sterile conditions.

See paragraph [0009] of the present application. This is different from the present invention in which the material transfer rates in the hollow fiber module according to the invention are lower at the start of the filtration process but are substantially higher on average over time than in the case of conventional devices in which severe fouling occurs in the course of time. See paragraph [0036] of the present application.

The prior art documents teach high packing densities to be most desirable in the application of membrane modules. Consequently, all prior work is focused on efficient anti-fouling methods when using high packing densities. Clearly, from what is disclosed in the prior art, one skilled in the art would not deduce to choose the opposite direction, that is, low packing densities, in order to solve a similar problem.

The advantages of low packing density are:

a) an improved average material transfer rate in the hollow fiber module over time of the filtration/dialysis process (see paragraph [0036] of the present application), and

b) a turbulent flow around the individual hollow fiber membranes, preventing the formation of deposits on the surfaces of the individual hollow fibers (see paragraph [0035] of the present application).

Zha et al

As will now be described in detail, the packing density of Zha et al is much higher than the present invention, and is outside of the range of the present claims. In fact, the packing density of Zha et al is of the order of the above prior art, which will result in fouling of the fiber membranes and a less efficient operation. Further, while the present invention seeks to provide membranes that "can also be arranged loosely next to one another" (paragraph [0031] at page 12 of the present application), the clear intention of Zha et al is to provide a membrane configuration with a maximum packing density, with the membranes "being arranged in close proximity to one another", as recited at column 2, lines 28-30 and 63-66 of Zha et al. Thus, Zha et al teaches away from the present invention.

The Examiner states that the definition of packing density in Zha et al is defined as the cross-sectional potted area taken up by the fiber membranes divided by the total potted area and is normally expressed as a percentage.

The Examiner further states that the term packing density in the present application refers to the ratio of the volume of all the hollow fiber membranes including their wall volume to the volume of the housing in which the hollow fibers are arranged, as defined in paragraph [0007] of the present application.

The essence of the rejection appears to be in the Examiner's statement in the paragraph spanning pages 7-8: "The examiner is unable to ascertain how the packing density of 5% in Zha ref would be equivalent to a packing density of 11% by the applicant's definition. Since the applicants have not provided the method as to how they arrived at this conclusion, the examiner sustains the rejection."

The following therefore explains how this conclusion as to the higher packing density of Zha et al was obtained.

It is first pointed out that, in the equations presented by the Examiner at page 7 of the Office Action, the denominator of the equation for Zha et al is <u>different</u> from the denominator of the equation for the present invention. This is because the "total cross-sectional potted area" of the Zha et al equation and the "cross-sectional area of housing" according to the present invention, are not the same.

In order to better understand this, reference is made to the drawing of enclosed Attachment A, which is a schematic cross-section of the cylindrical hollow fiber membrane module, as also shown in Fig. 4 of the present application. The segmentation elements have been omitted from the drawing for a better understanding, and the area which contains the segmentation elements and fiber membranes has been darkened.

Zha et al uses the "total potted area" for the definition of "packing density". The term "total potted area" in Zha et al means the area of the entire circle. Specifically, where r1 is the internal radius and r2 is the external radius, the "total potted area" refers to the entire circle of radius r2 which encompasses both the inner circle defined by radius r1 as well as the outer annulus defined by the difference in radii of r2 - r1. In other words, with reference to Attachment A, the "total potted area" of Zha et al refers to the combination of both the white inner circle and the black outer annulus. More specifically, the total potted area of Zha et al refers to the area $\pi(r2)^2$.

In the present invention, on the other hand, and referring to the drawing of Attachment A and Fig. 4 of the present application, the "area of housing" as used in the denominator of the respective formula on page 7 of the Office Action, means the area of the annulus only, that is, only the black annular in Attachment A. Specifically, the "area of housing" means the total potted area of Zha minus the inner white circle area of radius r1 (where no hollow fiber membranes are located). See Fig. 4 of the present application. In other words, the "area of housing" refers to the area $\pi(r2)^2 - \pi(r1)^2$. Paragraph [0007] refers to "the volume of the housing in which the hollow fibers are arranged," and the hollow fibers are only arranged in the black annular area of Attachment A.

Thus, the term "housing" as used by the inventors in their definition of "packing density" [paragraph 0007 of the present application], which is also clearly supported by the original language of the German priority document, means the volume of the compartments where the fiber membranes are located. This volume is much smaller compared to the volume of the entire cylinder according to Zha et al (entire potted area). Consequently, because the denominator of Examiner's formula for the present application is always smaller than the denominator of the Examiner's formula for Zha et al, the value of packing density according to the definition of the present invention is always greater than the packing density according to the definition of Zha et al.

As an example, assume that r2 = 8 cm, r1 = 6 cm and the same length is provided in both cases. In such case, the volume based on the total potted area according to Zha is about 2.29 times greater than the volume based on the annulus according to the present invention. Specifically, for a unit length, the volume in Zha et al is $\pi(r2)^2$ x length = 64π, whereas the volume of the present invention is $(\pi(r2)^2 - \pi(r1)^2)$ x length = $64\pi - 36\pi = 28\pi$. Therefore, the ratio of the volume of the total potted area divided by the volume of the present application is 64/28 = 2.29. Therefore, a packing density of 5% according to the Zha et al equation means about a 11.45% packing density by using the equation for the present application. In like manner, a packing density of 9% according to Zha et al translates to a packing density of about 20.6% by using the equation for the present application.

Therefore, Zha et al corresponds essentially to the known prior art discussed at paragraphs [0008], [0012] and [0030] of the present application.

In other words, if we substitute the denominator of the present application, which is 2.29 times less than the denominator of Zha et al, the packing density of Zha et al increases by 2.29%, and falls outside of the range of the present invention.

By using small packing densities in the present invention, a turbulent flow is provided over the individual hollow fiber membranes (paragraph [0036] of the present application), resulting a substantially higher material transfer during the filtration process compared to conventional techniques, including Zha et al. This is the case because the turbulent flow prevents the formation of deposits on the fiber membranes, which is otherwise termed "fouling." Zha et al, as with conventional prior art, discloses much more complicated mechanisms, such as gas flow around the fiber membranes, in order to prevent fouling (see paragraph [0012] of the present application).

Amendments to claims

In view of the above, in order to distinguish from Zha et al, claim 1 has been amended to recite that each housing includes an inner cylindrical space defined by a first outer radius (r1) and a surrounding annular packing space defined between a first inner radius equal to said first outer radius and a second outer radius greater than said first outer radius (r2 - r1), and the plurality of tubular hollow fiber membranes are arranged parallel to one another in the packing space only, wherein a volumetric ratio of all the hollow fiber membranes arranged in the packing space to the packing space (r2 - r1) inside the module is less than 10%.

Thus, claim 1 has been amended to define the packing space as only the black annular area in Attachment A, and the volumetric ratio has been provided only as to this packing space.

Thus, if we use the packing space of claim 1, which is 2.29 times less than the denominator of Zha et al, as the denominator in the equation for Zha et al to determine the "packing density," the packing density of Zha et al increases by 2.29%, and falls outside of the range of the present claimed application. As a result, Zha et al suffers from the same problems in the prior art, which are avoided by the present claimed invention.

Accordingly, it is respectfully submitted that the rejection of claims 1-4, 6, 10-12, 19, 21, 25 and 43 under 35 U.S.C. §102(e), has been overcome.

Claim 5 was rejected under 35 U.S.C. §103(a) as being obvious from U.S. Patent No. 6,524,481 to Zha et al.

The remarks made above in regard to Zha et al are incorporated herein, and are therefore not repeated.

Accordingly, for the same reasons given up, and since claim 5 depends from claim 1, it is respectfully submitted that the rejection of claim 5 under 35 U.S.C. §103(a), has been overcome.

Claims 13-16, 20 and 22-24 were rejected under 35 U.S.C. §103(a) as being obvious from U.S. Patent No. 6,524,481 to Zha et al in view of U.S. Patent No. 5,282,964 to Young et al.

The remarks made above in regard to Zha et al are incorporated herein, and are therefore not repeated.

Young et al fails to cure the deficiencies of Zha et al, and is therefore deficient

for this reason. The only disclosure in Young et al of packing density occurs at column 2, lines 36-37 where the prior art is discussed as increasing the packing density, contrary to the present claimed invention, and thereby teaching away from the present claimed invention.

Accordingly, it is respectfully submitted that the rejection of claims 13-16, 20 and 22-24 under 35 U.S.C. §103(a), has been overcome.

Claims 7-9, 26 and 42 were rejected under 35 U.S.C. §103(a) as being obvious from U.S. Patent No. 6,524,481 to Zha et al in view of European Patent Publication No. 1 008 358.

The remarks made above in regard to Zha et al are incorporated herein, and are therefore not repeated.

The European patent publication fails to cure the deficiencies of Zha et al, and is therefore deficient for this reason. The European patent publication is silent as to packing density.

Accordingly, it is respectfully submitted that the rejection of claims 7-9, 26 and 42 under 35 U.S.C. §103(a), has been overcome.

Claims 17, 18 and 44 were rejected under 35 U.S.C. §103(a) as being obvious from U.S. Patent No. 6,524,481 to Zha et al in view of U.S. Patent No. 5,282,964 to Young et al, as applied to claim 12 above, and further in view of U.S. Patent No. 4,689,255 to Smoot et al.

The remarks made above in regard to Zha et al and Young et al are incorporated herein, and are therefore not repeated.

Smoot et al fails to cure the deficiencies of Zha et al, and is therefore deficient for this reason. Smoot et al is silent as to packing density.

Accordingly, it is respectfully submitted that the rejection of claims 17, 18 and 44 under 35 U.S.C. §103(a), has been overcome.

Claim 47 was rejected under 35 U.S.C. §103(a) as being obvious from U.S. Patent No. 6,524,481 to Zha et al in view of U.S. Patent No. 6,251,275 to Rekers.

The remarks made above in regard to Zha et al are incorporated herein, and are therefore not repeated.

Rekers fails to cure the deficiencies of Zha et al, and is therefore deficient for this reason. Rekers is silent as to packing density.

Accordingly, it is respectfully submitted that the rejection of claim 47 under 35 U.S.C. §103(a), has been overcome.

In addition to the above, claim 24 has been canceled, in view of the reduced percentage already recited in claim 1.

Further, claims 7, 11, 12, 15-17, 21, 26 and 47 have been amended in formal respects to provide proper antecedent basis.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

In the event that this Paper is late filed, and the necessary petition for extension of time is not filed concurrently herewith, please consider this as a Petition for the requisite extension of time, and to the extent not tendered by check attached hereto, authorization to charge the extension fee, or any other fee required in connection with this Paper, to Account No. 08-2525.

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The Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 08-2525.

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 1-23, 25, 26, 42-44 and 47 are allowable, and early and favorable consideration thereof is solicited.

Respectfully submitted,

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Attachment: Appendix A

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APPENDIX A

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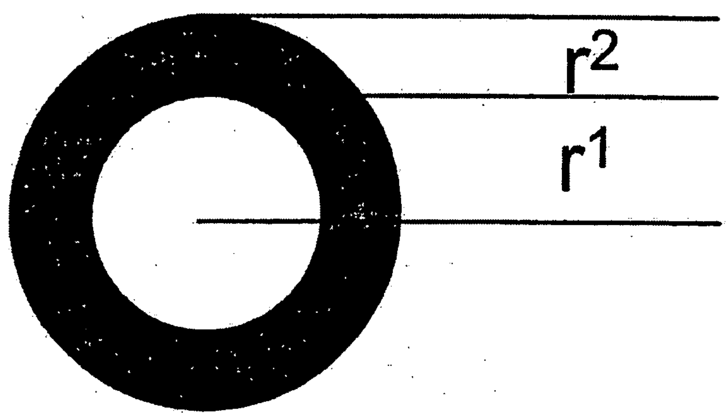

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